REMARKS

Obviousness-Type Double Patenting

Claims 58, 59, 63, 64, 67-72, 75-76, 84-86, 94-96 and 115-157 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-4, 6-14, 18-56, and 69-75 of U.S. Patent 5,981,505 .

Applicants respectfully disagree. However, to further the prosecution of the present application, Applicants may file a terminal disclaimer upon indication of allowability of the claims.

Claims 58, 59, 63, 64, 67-72, 75-76, 84-86, 94-96 and 115-157 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-7, 12-15, 17-19, and 21-23 of U.S. Patent 5,739,118. Applicants respectfully disagree.

U.S. Patent 5,739,118 claims 1-7, 12,-15, and 17-19 all claim inventions that comprise saponin. However, the claims of the present application do not claim saponin and there is no suggestion or motivation within the claims to use saponin. Therefore, Applicants respectfully request that the rejection under the judicially created doctrine of obviousness-type double patenting be withdrawn.

Claims 58, 59, 63, 64, and 122-125 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 18-24 and 30-32 of U.S. Patent 5,817,637.

Applicants respectfully disagree. However, to further the prosecution of the present application, Applicants may file a terminal disclaimer upon indication of allowability of the claims.

Claims 67-72, 75-76, 84-86, 94-96,115-121, and 126-157 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-7 and 14-17 of U.S. Patent 5,830,876.

Applicants respectfully disagree. However, to further the prosecution of the present application, Applicants may file a terminal disclaimer upon indication of allowability of the claims.

Claims 67-72, 75-76, 84-86, 94-96, 115-121, and 126-157 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-4 of U.S. Patent 5,593,972 .

Applicants respectfully disagree. However, to further the prosecution of the present application, Applicants may file a terminal disclaimer upon indication of allowability of the claims.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 58, 59, 63, 64, 67-72, 75, 76, 84-86, 94-96, and 115-157 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner alleges that, "While applicants have shown a composition comprising DNA and a polynucleotide function enhancer, the only data presented are model systems which are not predictive of success in production of a pharmaceutical vaccine with a pharmaceutical composition comprising DNA and a polynucleotide function enhancer. In order to do so undue experimentation is required." (Office Action, page 7) Applicants respectfully disagree and request that the rejection be reconsidered and withdrawn.

Claims 148-157

Although the Examiner rejected claims 148-157 under 35 U.S.C. § 112, first paragraph, along with the other claims cited above, the argument that the Examiner used to reject claims 148-157 has no basis. The Examiner appears to suggest that the claims that are currently pending are only useful for a DNA vaccine that provides protective immunity and since the field of DNA vaccines is allegedly unpredictable all the claims

are rejected under 35 U.S.C. § 112, first paragraph. This is clearly incorrect. Claim 148 reads in part, "A method of ***inducing antibodies*** against an antigen ..." (emphasis added). Claims 149-157 are dependent claims that are dependent upon claim 148. Applicants remind the examiner that it is the ***claimed*** invention that must be enabled. Thus, Applicants must enable the induction of antibodies upon administration of DNA, as recited in claim 148. There is clear support for claims 148-157 throughout the specification (see, for example page 3, page 7 lines 35-38, page 2 lines 40-42, and Examples 3 and 4 beginning on page 42 of the specification).

Induction of antibodies in response to an antigen is well within the ability of those skilled in the art and does not require undue experimentation as the Examiner suggests. With the teachings set forth in the specification and the knowledge of one of ordinary skill in the art, the art-skilled can induce antibodies against an antigen following the method that is described in claims 148-157. Accordingly, claims 148-157 are amply enabled.

Claims 58, 59, 63, 64, 67-72, 75, 76, 84-86, 94-96, and 115-147

As to claims 58, 59, 63, 64, 67-72, 75, 76, 84-86, 94-96, and 115-147 and the Examiner's allegation that it would require "undue experimentation" to use the invention, Applicants respectfully disagree. The Examiner suggests that the invention requires "undue experimentation" because the present application does not satisfy the *Wands* factors. The Examiner suggests that the art of DNA vaccines is highly unpredictable and, thus, requires explicit teachings.

One skilled in the art would accept Applicants' assertions to the PTO and the numerous scientific publications to which Applicants refer to support these assertions. Additionally, the patent office has issued approximately 130 patents in the area of DNA vaccines since 1996 (see, for example, the attached document from http://www.dnavaccine.com/Patents/patent.html).

The Examiner suggests that the statement "[in] common with traditional vaccine, though, current genetic approaches will probably have to be combined in many cases with generalized immune stimulators (adjuvants) in order to elicit the strong immune responses required to shield recipients from future infections, shows that a great deal of

experimentation is common to all vaccine production." However, the Federal Circuit has repeatedly stated that the amount of experimentation is not the relevant test, but rather whether it is a burden or ***undue*** experimentation. Routine experimentation does not constitute undue experimentation.

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention.

PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 U.S.P.Q.2d 1618, 1623 (Fed. Cir. 1996) (quotation and citation omitted). Experimentation may be required to get some vaccines to work, but the basic technology is sound. The experimentation that would be undertaken by the art-skilled to determine the precise conditions that are required to provide a protective immune response is routine. The art-skilled know how to vary the adjuvant, the amount of antigen, and other factors that are required when formulating a vaccine. What the present invention provides is how to administer a DNA vaccine and what the pharmaceutical composition should be, knowledge that the art-skilled lacked until the present invention. The Examiner is reminded that the PTO does not act as the FDA.

The Examiner also suggests that the absence of working examples of a vaccine in the application is another factor that would require one of ordinary skill in the art to perform undue experimentation. Applicants respectfully disagree. It is well accepted case law that an application ***does not*** need working examples in the application. The instant application provides sufficient guidance to enable those skilled in the art to practice the invention.

The Examiner further suggests that the nature of the invention is complex. The Examiner states, "The use of DNA for immunization and passive protection is a new and developing art[.]" However, this in contrast to evidence that can be obtained directly from the United States Patent and Trademark Office. As discussed above the USPTO has granted approximately 130 patents in the area of DNA vaccine technology since 1996.

Although, the field of DNA vaccines is a relatively new field when compared to other vaccine technologies, this does not mean that the invention is more complex. The Examiner appears to focus on the words of Cho *et al.* where the author states, "With all of these disadvantages, one might wonder why investigators remain so interested in the prospect of using macromolecules as drugs." However, the number of disadvantages is irrelevant to establish enablement and patentability, rather the standard is whether one skilled in the art would accept the assertions made in the present application and the answer is unequivocally, ***yes***.

It should be pointed out that DNA vaccines have been proven to work in primates. Applicants submitted a declaration in response to a previous office action that demonstrated the efficacy of their DNA vaccine technology. The DNA vaccine protected completely 1 out 4 monkeys (25%) and induced an immune response in 2 out 4 (50%) monkeys. Therefore, in the primates treated with the pharmaceutical composition administered following the methods that are claimed, 75% of the primates were either completely protected or partially protected. Furthermore, many other biotechnology and pharmaceutical companies have also shown success using DNA vaccines to protect animals against diseases like HIV. Thus, the field of DNA vaccines is not overly complex and has been proven to work in higher animals, such as chimpanzees.

The Examiner also alleges that there is great unpredictability of DNA vaccines. As with most medical research, the outcome of an experiment or procedure is never 100% certain. To practice the present invention, the art-skilled can follow the teachings in the present specification to formulate a pharmaceutical composition that can have various uses. It is clear from the specification that the claimed composition will produce antibodies when administered to an individual. It is also clear from the declaration, that was previously submitted, that the composition can work as a vaccine. Further, even though DNA vaccines may be considered by some to be a new field and optimization may be needed in some cases, it is well accepted that DNA vaccines work and provide at least some benefit in generating an immune response. Thus, those skilled in the art would accept the assertions that DNA vaccines are useful, as has the PTO as evidenced by the number of patents that have been issued in the area of DNA vaccines.

Therefore, the present application is completely enabled and ***does*** teach how to make and use the present invention. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. §112, first paragraph be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 115-118, 120, and 121 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by WO 91/12329. The Examiner alleges that WO 91/12329 discusses a method of introducing a DNA molecule and a polynucleotide enhancer to cells of a host and that the DNA molecule may be a plasmid and the site of introduction may be skeletal muscle. Applicants respectfully disagree.

The standard for anticipation under 35 U.S.C. § 102(b) is one of strict identity. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference, *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984).

WO 91/12329 reports the introduction of genetic material into a cell. However, the WO 91/12329 only discusses the introduction of genetic material into a cell using a retroviral vector and a chemical agent. WO 91/12329 does not discuss or disclose the introduction of a DNA plasmid with a chemical agent into muscle as the Examiner alleges. A retroviral vector does not contain DNA. The specification of WO 91/12329 discloses that a "retroviral vector is a retrovirus," (page 17 , line 17) and further states that "Retroviruses are RNA viruses, that is, the viral genes are encoded in an ***RNA molecule rather than in a DNA molecule.***" (page 8, lines 32-34).

Thus, WO 91/12329 does not disclose each limitation of a claim and therefore cannot anticipate the present invention. Therefore, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 58,59, 63, 64, 67-72, 75, 76, 84-86, 94-96, and 115-157 stand rejected under 35 U.S.C § 103(a) as allegedly being unpatentable over U.S. Patent 6,214,804 (hereinafter the "'804 patent") in view of Price *et al.* and WO 91/12329. The Examiner alleges that the '804 patent discusses a method of introducing a pathogenic antigen into

an individual for the production of an immune response including the production of antibodies, but does not discuss a polynucleotide function enhancer. The Examiner alleges that WO 91/12329 discusses introducing a DNA molecule and polynucleotide function enhancer to cells of a host and that Price *et al.* discusses the plasmid of WO 91/12329 encoded a viral antigen from an intracellular pathogen. The Examiner concludes that it would have allegedly been obvious to combine the teachings of the above mentioned references to get the claimed inventions. Applicants respectfully disagree.

As is clear from MPEP §2143, in order to provide a *prima facie* case of obviousness, the Examiner must first establish motivation to combine or modify the references.

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

MPEP §2143. The Examiner cannot rely upon a reasonable expectation of success alone to establish motivation. Such reliance is improper.

As discussed above, WO 91/12329 does not discuss the introduction a DNA molecule and polynucleotide function enhancer into a cell. In fact, WO 91/12329 teaches away from using DNA, but rather focuses almost exclusively on using retroviruses, i.e. RNA. WO 91/12329 states, "The treatment of genetically-related diseases with techniques as DNA transfection has thus far, unfortunately, not met with great success." (page 7, lines 24-26). The specification goes on to describe the extreme limitations of using DNA techniques and does not discuss introducing DNA with a polynucleotide function enhancer. A reference that teaches away from using a claimed element of an invention cannot be properly combined with another reference to establish a *prima facie* case of obviousness. It is impermissible to pick and chose among a publication's teachings.

Even if the '804 patent was combined with WO 91/12319 or Price *et al.* the claimed invention is not produced. A person of ordinary skill in the art combining these two references would use a retrovirus and a chemical agent. As stated above, there is no suggestion in WO 91/12319 to use ***DNA*** and the chemical agent, but rather to use RNA-comprising viruses. Thus, if a person of ordinary skill in the art were motivated to combine the references, which that person is not, the art-skilled would not be in possession of the pharmaceutical compositions that are disclosed in the Applicants' application.

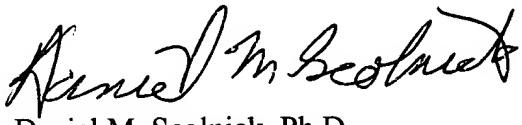
Therefore, there is no *prima facie* case of obviousness because there is no motivation to combine the references because none of the references suggest the combination or refer to the other references explicitly or implicitly and even if the combination were made the combination does not produce the Applicants invention.

Accordingly, Applicants respectfully request the rejection under 35 U.S.C. § 103(a) be withdrawn.

Conclusion

Claims are in condition for allowance. An indication of allowability is therefore earnestly solicited. Applicant invites the Examiner to contact the undersigned at (215) 665-6928 to clarify any unresolved issues raised by this response.

Respectfully submitted,



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Attachments: Printout http://www.dnavaccine.com/Patents/patent.html